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APPLICATION NO.	FILING DATE	FIRST-NAMED INVENTOR	ATTORNEY DOCKET NO.
09/183,789	10/30/98	MARTELANGE V	[illegible]

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EXAMINER	ART UNIT	PAPER NUMBER
HARRIS,	[illegible]	12

DATE MAILED: 05/09/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/183,789	Martelange et al.
Examiner	**Group Art Unit**
Alana M. Harris, Ph. D.	1642

☒ Responsive to communication(s) filed on *March 7, 2000.*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1, 8, 9, 18-20, 24, 28, 35, 38, 40, 41, 43, 45, 47, and 50-59* is/are pending in the applicat

Of the above, claim(s) *20, 24, 28, 35, 38, 45, and 47* is/are withdrawn from consideration

☒ Claim(s) *1, 8, 9, 18, 19, 40, 41, 43, and 50-59* is/are allowed.

☐ Claim(s) _____ is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *11* & 4

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

1. Applicant's election without traverse of Group I (claims 1, 8, 9, 18, 19, 40, 41 and 43) in Paper No. 10 is acknowledged.

2. Claims 51-59 have been added.

Claims 2-7, 10-17, 21-23, 25-27, 29-34, 36, 37, 39, 42, 44, 46, 48 and 49 are canceled.

Claim 50 has been amended.

Claims 1, 8, 9, 18-20, 24, 28, 35, 38, 40, 41, 43, 45, 47 and 50-59 are pending.

Claims 20, 24, 28, 35, 38, 45 and 47, drawn to non-elected inventions are withdrawn from examination.

Claims 1, 8, 9, 18, 19, 40, 41, 43, 50 and 50-59 are examined on the merits.

Priority

3. Acknowledgment is made of applicant's claim for priority under 35 U.S.C. § 120. The Examiner has reviewed U. S. Application Serial Number 09/060,706, filed April 15, 1998. While SEQ. ID. #1 is disclosed in aforementioned application, the limitations of sequences, SEQ. ID. #38, 40 and 43 are not disclosed in U.S. Application No. 09/060,706 from which priority is claimed. Thus, the pending claims (1, 8, 9, 18, 19, 40, 41, 43, 50 and 52-59) will not be granted

the April 15, 1998 priority date. Priority of claims (1, 8, 9, 18, 19, 40, 41, 43, 50 and 52-59) will be granted the effective filing date of the instant application filed on October 30, 1998. Priority of claim 51 will be granted to U.S. Application No. 09/060,706, filed April 15, 1998.

Specification

4. The disclosure is objected to because of the following informalities: it contains embedded hyperlinks or other forms of browser-executable code listed on page 12 that is impermissible and requires deletion (see M.E.P.. 608.01(p)) and the specification is incomplete for lacking a period at the end of a sentence on page 1, line 27. It is not clear whether other text is missing. Applicant is advised to review the entire specification for similar errors. Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 8, 9, 18, 19 and 51-56 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 8, 9, 18, 19 and 51-56 are broadly drawn to isolated nucleic acid molecules encoding a sarcoma associated gene (SAGE) product consisting of: SEQ ID NO:38 and SEQ ID NO:43, deletions, additions, substitutions and complements (claim 1), SEQ ID NO:1, nucleotides 119-1831 of SEQ ID NO:38 and nucleotides 79-1659 of SEQ ID NO:43 (claim 8), unique fragments of 1-1997 of SEQ ID NO:38 between 12 and 1996 nucleotides in length and 1-2442 of SEQ ID NO:43 between 12 and 2441 nucleotides in length and complements (claim 9), expression vector contained in a host cell comprising claimed nucleic acids (claims 18 and 19) and nucleic acid sequence set forth as SEQ ID NO:1, 38, 40, 43 and the recited nucleotides (claims 51-56). Thus, all cited claims are broadly drawn to a genus of nucleic acid molecules that encompass a larger nucleic acid that encode sdp3.10 (SAGE), sdp3.5 polypeptides and not excluding tumor rejection antigen precursors (TRAPs) and TRAs (derived from TRAPs). The specification on page 28 describes only the art known components of a gene such as a TATA box and 5' non-transcribing regulatory sequences, the specification does not describe any of the structural elements of a gene that would encode these actual DNA sequences of promoter and regulatory regions and introns, all defining elements of a "gene". The specification lacks information to lead one of skill in the art to understand that the applicant had possession of the broadly claimed invention at the time the instant application was filed. Thus, one of skill in the art would not understand that the applicant had possession of the claimed invention at the time the instant application was filed. Applicant is referred to the revised interim guidelines concerning

compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Likewise, the specification does not contain any disclosure of the function of a full length open reading frame (ORF) that includes SEQ ID NO:38, 43 and their specified unique fragments. The genus of cDNAs including SEQ ID NO:1, 38, 40 and 43 is very large and members of the genus are variable because of the potentiality of the many different proteins they may encode. Therefore, many structurally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. One skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

7. Claim 40 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 40 is broadly drawn to "A composition comprising: an antisense molecule which binds to a tumor associated nucleic acid molecule...and reduces the expression of the tumor associated nucleic acid...". Claims drawn to compositions comprising antisense nucleic acids are broadly interpreted to read on compositions effective for use as *in vivo* human therapeutics. The nucleic acids of the invention are completely uncharacterized functionally. The mere facts that it seems to be expressed in cancerous tissues, can be an essential event in the process of tumorigenesis and associated with the development of several different types of cancer is not

sufficient to establish that it plays a role in the pathology or etiology of diseases in these tissues. In the absence of an established role of the polypeptide in cancerous diseases other than in the specified excluded organ/tissue systems listed on pages 6 and 7 of the specification is not certain what if any therapeutic effect the administration of the antisense molecule would have for the treatment of the balance of diseased organ/tissue systems. The selection and development of such human therapeutics is art known to be highly unpredictable. The specification exemplifies no examples of the effective use of the effective use of the polypeptide as a pharmacological agent and no such uses are art known. Could these claimed proteins reasonably be selective and specific in their application of treating or preventing cancer when according to the specification to be **associated** with the development of cancer? Accordingly, those skilled in the art cannot rely on this information to implement the processes of treating or preventing a number of types of cancer, such as adenocarcinoma, leukemia or melanoma. One skilled in the art would not know how to use the claimed compositions as the component polypeptides were not known prior to the applicant's invention. Its function is not known and is not disclosed in the specification, which speculates merely that it is "associated" with the development of cancer. The specific association is not elucidated. None of the "associated" nucleotides and antisense nucleic acid claimed are known to be useful for the treatment or prevention of cancer.

Furthermore, Rojanasakul (Advanced Drug Delivery Reviews 18:115-131, 1996) states "...[oligonucleotides] effective use has been limited due to several problems...these compounds are poorly taken up by cells and therefore may not reach their target site. Moreover, problems

associated with cellular targeting, potential toxicity, and affinity of [oligonucleotides] to the target sites pose major challenges to the successful utilization of these compounds." Granted their are potential advantages of antisense therapy, however there are many challenges that exist in the application of antisense technology to humans. Therefore, due to the unpredictability of therapeutics and the absence of any evidence concerning the effectiveness of the claimed composition as a pharmacological agent, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use with a reasonable expectation of success, the invention commensurate in scope with this claim. The association provides no guidance as to how the instant antisense nucleic acid can be employed as therapeutic nor a basis to predict its efficacy.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1, 18, 19, 40, 41, 43, 51-58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The recitation "...hybridize under stringent..." in claims 1 and 40 is not clear. The metes and bounds are unclear and in the absence of limitations specifying specific stringency conditions.

b. Claim 40 is vague and indefinite in the recitation "...reduces the expression...". It is not clear how to interpret the term reduces. Is reduction defined for example as the total abolishment of the tumor associated nucleic acid or a specific percentage less than expression in the normal tissue counterpart? The metes and the bounds of the claim cannot be determined.

c. The recitation "...polypeptide precursor..." in claims 41 and 43 is vague and indefinite. The recitation is unclear in what is defined as a polypeptide precursor. Is it for example an amino acid, mRNA? There is a complete lack of characterization of the recitation.

d. Claims 57 and 58 are vague and indefinite in the recitation "...at least a portion...". It is not clear as to what is defined as a portion, half of the designated nucleic acid, a couple of nucleotides or the entire sequence minus one of two bases? Accordingly, the metes and bounds are unclear.

Claim Rejections - 35 U.S.C. § 101

10. Claims 1, 8, 9, 18, 19 and 51-56 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility, a credible or a well established utility.

The applicant has asserted several utilities for the claimed nucleic acid molecules. The specification asserts the following utilities for the claimed nucleic acid molecules, consisting of SEQ ID NO:1, SEQ ID NO:38, SEQ ID NO:40, SEQ ID NO:43, as well as fragments of each sequence: probes, amplification primers for determining expression, and in the manufacture of

medicaments and diagnostics. However, these asserted utilities are not credible, specific or substantial. The broadly claimed nucleic acids are based on the aforementioned sequence identification numbers that encode "tumor rejection antigen precursors", sdph3.10 (SAGE) and sdp3.5 polypeptides. Other than the nucleotide sequence identification numbers, the reference of their subsequent polypeptide products and given lab designation acronyms, the specification provides no functional characterization of the subsequent polypeptides, no specific tissue distribution of the expression of the polynucleotides, except not in tissues such as the testis, bladder or ovary (pages 6-9). However, there would be a number of other tissues expression would not be limited to such as the breast, pancreas or brain, as well as a number of sarcomas and carcinomas as listed on page 11, lines 14 and 15 of the specification. Consequently there is know information that links expression of the resulting **merely** tumor **associated** polypeptides to any specific tissue. Thus, the asserted utility of the claimed nucleic acids is not substantial, specific or credible.

Claims 1, 8, 9, 18, 19 and 51-56 are also rejected under 35 U.S.C., first paragraph. Specifically, since the claimed invention is not supported by either and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 U.S.C. § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

12. Claims 1, 9, 18, 19, 50 and 59 are rejected under 35 U.S.C. 102(b) as being anticipated by Accession Number U89672 (March 21, 1997) and Rees et al. (BioTechniques 20:102-110, 1996). Accession #U89672 and Rees et al. disclose an isolated nucleic acid molecule selected from the group consisting of:

(a) nucleic acid molecules which hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence selected from the group consisting of SEQ ID NO:38, which codes for a sarcoma associated gene product,

(b) deletions, additions and substitutions of the nucleic acid molecules of (a),

(c) nucleic acid molecules that differ from the nucleic acid molecules of (a) or (b) in codon sequence due to the degeneracy of the genetic code,

(d) complements of (a), (b) and (c),

(e) a unique fragment of the nucleotide sequence set forth as nucleotides 1-1997 of SEQ ID NO:38 between 12 and 1996 nucleotides in length and

(f) complements of (e), the same as that claimed in claims 1 and 9.

Rees et al. also disclose a host cell that is transfected with an expression vector comprising the isolated nucleic acid molecule of claim 1 that is operably linked to a promoter (claims 18 and 19). Additionally disclosed are methods for producing a tumor associated polypeptide comprising expressing in an expression system the expression vector of claim 18, isolating the tumor associated polypeptide or a fragment thereof from the expression system, culturing the isolated host cell of claim 19 and isolating the tumor associated polypeptide or a fragment thereof from the expression system (claims 50 and 59).

13. Claims 1, 9, 18, 19, 50 and 59 are rejected under 35 U.S.C. 102(b) as being anticipated by Accession Number AA213817 (August 13, 1997). Accession #AA213817 discloses an isolated nucleic acid molecule selected from the group consisting of:

(a) nucleic acid molecules which hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence selected from the group consisting of SEQ ID NO:43, which codes for a sarcoma associated gene product,

(b) deletions, additions and substitutions of the nucleic acid molecules of (a),

(c)nucleic acid molecules that differ from the nucleic acid molecules of (a) or (b) in codon sequence due to the degeneracy of the genetic code,

(d) complements of (a), (b) and (c),

(e) a unique fragment of the nucleotide sequence set forth as nucleotides 1-1997 of SEQ ID NO:43 between 12 and 2441 nucleotides in length and

(f) complements of (e), the same as that claimed in claims 1 and 9.

Rees et al. also disclose a host cell that is transfected with an expression vector comprising the isolated nucleic acid molecule of claim 1 that is operably linked to a promoter (claims 18 and 19). Additionally disclosed are methods for producing a tumor associated polypeptide comprising expressing in an expression system the expression vector of claim 18, isolating the tumor associated polypeptide or a fragment thereof from the expression system, culturing the isolated host cell of claim 19 and isolating the tumor associated polypeptide or a fragment thereof from the expression system (claims 50 and 59).

14. Claims 1, 9, 18, 19, 50 and 59 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Number 5,880,102 (filed Jan. 17, 1995). Sequence #1 of U.S. Patent #5,880,102 discloses an isolated nucleic acid molecule selected from the group consisting of:

(a) nucleic acid molecules which hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence selected from the group consisting of SEQ ID NO:38, which codes for a sarcoma associated gene product,

(b) deletions, additions and substitutions of the nucleic acid molecules of (a),

(c)nucleic acid molecules that differ from the nucleic acid molecules of (a) or (b) in codon sequence due to the degeneracy of the genetic code,

(d) complements of (a), (b) and (c),

(e) a unique fragment of the nucleotide sequence set forth as nucleotides 1-1997 of SEQ ID NO:38 between 12 and 1996 nucleotides in length and

(f) complements of (e), the same as that claimed in claims 1 and 9.

Rees et al. also disclose a host cell that is transfected with an expression vector comprising the isolated nucleic acid molecule of claim 1 that is operably linked to a promoter (claims 18 and 19).Additionally disclosed are methods for producing a tumor associated polypeptide comprising expressing in an expression system the expression vector of claim 18, isolating the tumor associated polypeptide or a fragment thereof from the expression system, culturing the isolated host cell of claim 19 and isolating the tumor associated polypeptide or a fragment thereof from the expression system (claims 50 and 59).

15. Claims 1, 9, 18, 19, 50 and 59 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Number 5,464,745 (filed March 31, 1993). Sequence #1 of U.S. Patent #5,434,745 discloses an isolated nucleic acid molecule selected from the group consisting of:

(a) nucleic acid molecules which hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence selected from the group consisting of SEQ ID NO:43, which codes for a sarcoma associated gene product,

(b) deletions, additions and substitutions of the nucleic acid molecules of (a),

(c) nucleic acid molecules that differ from the nucleic acid molecules of (a) or (b) in codon sequence due to the degeneracy of the genetic code,

(d) complements of (a), (b) and (c),

(e) a unique fragment of the nucleotide sequence set forth as nucleotides 1-1997 of SEQ ID NO:38 between 12 and 2441 nucleotides in length and

(f) complements of (e), the same as that claimed in claims 1 and 9.

Rees et al. also disclose a host cell that is transfected with an expression vector comprising the isolated nucleic acid molecule of claim 1 that is operably linked to a promoter (claims 18 and 19). Additionally disclosed are methods for producing a tumor associated polypeptide comprising expressing in an expression system the expression vector of claim 18, isolating the tumor associated polypeptide or a fragment thereof from the expression system, culturing the isolated host cell of claim 19 and isolating the tumor associated polypeptide or a fragment thereof from the expression system (claims 50 and 59).

Claim Rejections - 35 U.S.C. § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claims 41 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Accession #U89672, Rees et al. or U.S. Patent #5,880,102 teach the isolated nucleic acid of claim 1comprising a first isolated nucleic acid molecule consisting of a 12-32 nucleotide contiguous segment of SEQ ID NO:38, and a second isolated nucleic acid molecule consisting of a 12-32 nucleotide contiguous segment of the complement of SEQ ID NO:38, wherein the contiguous segments are nonoverlapping and the first and second isolated nucleic acid molecules are constructed and arranged to selectively amplify at least a portion of an isolated nucleic acid molecule comprising SEQ ID NO:38. The aforementioned references do not teach a kit for detecting the presence of the expression of a tumor associated polypeptide precursor.

However, although the claim recites a kit, no positive recitation of the kit ingredients/elements distinguishes the claim over the references. Therefore, the references read on the claimed kit. Further, it is a well-known convention in the art to place the recited elements in a kit for the advantages of convenience and economy, and methods of detecting polypeptide expression also were well known and available to the ordinarily skilled artisan. Thus, the claimed subject matter is considered obvious over the prior art, absent sufficient factual evidence to the contrary.

18. Claims 43 and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Accession #AA213817 or U.S. Patent #5,434,745 teach the isolated nucleic acid of claim 1comprising a first isolated nucleic acid molecule consisting of a 12-32 nucleotide contiguous segment of SEQ ID NO:43, and a second isolated nucleic acid molecule consisting of a 12-32 nucleotide contiguous segment of the complement of SEQ ID NO:43, wherein the contiguous segments are nonoverlapping and the first and second isolated nucleic acid molecules are constructed and arranged to selectively amplify at least a portion of an isolated nucleic acid molecule comprising SEQ ID NO:43. The aforementioned references do not teach a kit for detecting the presence of the expression of a tumor associated polypeptide precursor.

However, although the claim recites a kit, no positive recitation of the kit ingredients/elements distinguishes the claim over the references. Therefore, the references read on the claimed kit. Further, it is a well-known convention in the art to place the recited elements in a kit for the advantages of convenience and economy, and methods of detecting polypeptide expression also were well known and available to the ordinarily skilled artisan. Thus, the claimed subject matter is considered obvious over the prior art, absent sufficient factual evidence to the contrary.

19. Claims 8, 40 and 51-56 are free of the art.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris whose telephone number is (703) 306-5880. The examiner can normally be reached on Monday through Friday from 7:00 am to 3:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Alana M. Harris, Ph.D.
Patent Examiner, Group 1642
May 7, 2000

YVONNE EYLER, PH.D
PRIMARY EXAMINER